Nebraska Department of Health and Human Services

HEALTH ALERT NETWORK

Update

TO: Nebraska Healthcare Providers, Local Health Departments, and Veterinarians

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RE: Update: Fungal Infections Resulting from Contaminated Pharmaceuticals prepared by the New England Compounding Center (NECC), Framingham, Massachusetts (HAN #3)

DATE: October 18, 2012

Public health authorities throughout the United States are carefully tracking infectious complications related to the use of injectable pharmaceuticals produced by and shipped from the New England Compounding Center (NECC) in Framingham, Massachusetts. As of October 18, 2012, no evidence exists to confirm that Nebraska providers or facilities have received products known to be contaminated or implicated to have caused infections in patients elsewhere. We are continuing to monitor developments carefully regarding this issue, and will notify Nebraska health care providers/facilities as the situation warrants.

NECC is registered and licensed to ship products to Nebraska and we have acquired records listing all products shipped from NECC to Nebraska health care providers and facilities since May 2011. **While no products shipped to the approximately 29 Nebraska locations are currently implicated as having been contaminated or demonstrated to have caused infections, all NECC products are under an FDA recall (please see the last page of this HAN for a list of facilities).** Nebraska's local health departments will be notifying facilities within their respective jurisdictions who received such products to verify removal from inventories and to provide information for assessment, care, and management of patients to whom NECC products were administered. The current recommendation is to contact any patient receiving a NECC-supplied injectable medication on or after May 21, 2012.

Because fungal infections can be slow to develop, clinicians should continue to monitor for symptom onset in patients who have received injectable medication from this pharmacy. In this outbreak, symptoms typically have appeared 1 to 4 weeks following injection. However, longer and shorter periods of time between injection and onset of symptoms have been reported. Therefore, patients and physicians should remain vigilant for symptoms for several months following injection(s).
We will continue to monitor this situation closely and will provide pertinent updates to the Nebraska health care community as the situation warrants.

ERRATUM: On October 5, 2012 we issued HAN #1 providing initial notification of implicated products from the NECC Compounding Pharmacy. An Update (HAN #2) was distributed on October 09, 2012. Because of a computer error, HAN #1 was inadvertently re-distributed on October 16, 2012. We regret any confusion this may have caused. All HANs distributed by our agency are archived here: http://dhhs.ne.gov/publichealth/Pages/han_archive.aspx

This is an official
CDC Health Advisory

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CDCHAN-00329-2012-10-17-UPD-N

Update: Multistate Outbreak of Fungal Meningitis and Joint Infections Associated with Contaminated Steroid Medications

Summary

The Centers for Disease Control and Prevention (CDC) and the Food and Drug Administration (FDA) continue to work closely with state public health departments on a multistate investigation of fungal meningitis and joint infections among patients who received a methylprednisolone acetate injection prepared by the New England Compounding Center (NECC) in Framingham, Mass. Some of these patients who received epidural injections also suffered strokes that may have resulted from their infection. This HAN notice provides updated information on the following:

- Status of the investigation.
- FDA issuance of a MedWatch Safety Alert on October 15 advising clinicians to follow-up with patients who received an injectable NECC product, including any ophthalmic drug that is injectable or used in conjunction with eye surgery, and a cardioplegic solution purchased from or produced by NECC after May 21, 2012.
- Recommendations for clinicians.
- Case definition.

Background

CDC, in collaboration with FDA, state public health departments, and state boards of pharmacy, has been investigating an ongoing outbreak of fungal infections associated with a contaminated steroid medication, preservative-free methylprednisolone acetate (80mg/ml) prepared by the New England Compounding Center, in Framingham, Mass. CDC and state public health departments are actively coordinating outreach to patients who have been exposed to this contaminated medication.

As of October 16, 2012, a total of 233 cases, which includes 2 peripheral joint infections and15 deaths, have been reported in 15 states (see CDC's website for up-to-date information about case count and distribution by state). The fungus *Exserohilum rostratum* has been reported in clinical specimens from multiple patients with fungal meningitis and with other spinal infections (e.g., epidural abscess). CDC and FDA continue to investigate the possibility of contamination with additional organisms. At this time, one clinical specimen has tested positive for the fungus *Aspergillus fumigatus*, and another has tested positive for the fungus *Cladosporium*. Fungal meningitis is not transmitted from person to person.

The clinical presentation of infected patients with fungal meningitis remains consistent with that described in previous reports: onset of symptoms is typically between 1 to 4 weeks following injection with a variety of symptoms, including fever, new or worsening headache, nausea, and new neurological deficit (consistent with deep brain stroke). However, fungal infections can be slow to develop, and there are reports of longer periods between injection and onset of symptoms; and, therefore, patients and their doctors need to watch closely for symptoms for at least several months following the injection. Some of these patients' symptoms were very mild in nature. Cerebrospinal fluid (CSF) obtained from these patients has typically had an elevated white cell count (usually with a predominance of neutrophils), and in many cases low glucose and elevated protein. As of October 16, two peripheral joint infections have been reported. CDC expects that through ongoing patient notification efforts, additional patients with infections of the joints may come forward.

On September 26, 2012, NECC voluntarily recalled the following lots of methylprednisolone acetate (PF) 80mg/ml:

- Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #05212012@68, BUD 11/17/2012
- Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #06292012@26, BUD 12/26/2012
- Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #08102012@51, BUD 2/6/2013

On October 6, NECC expanded its previous recalls to include all products currently in circulation that were compounded at and distributed from its facility in Framingham, Mass. More information about this recall is available at the FDA website.

All cases reported as of October 16 have occurred after injections with methylprednisolone acetate products from one of the three lots recalled on September 26.

FDA MedWatch: Additional NECC Products of Potential Concern

On October 15, FDA released a MedWatch Safety Alert announcing that, as a result of the ongoing investigation of NECC, a patient with possible fungal meningitis who had received an epidural injection of triamcinolone acetonide produced by NECC has been identified through active surveillance efforts by CDC and state health departments and reported to FDA. Triamcinolone acetate is a type of steroid injectable product made by NECC. As of October 17, there is no laboratory evidence of fungal infection in this patient. As noted above, all cases of fungal meningitis identified to date have been associated with methylprednisolone acetate, another similar steroid injectable product distributed by NECC.

In addition, FDA received a report of one cardiac transplant patient with *Aspergillus fumigatus* infection who was administered NECC cardioplegic solution, which is used to prevent injury to the heart during surgery. Investigation of this patient is ongoing; there may be other explanations for this patient's *Aspergillus* infection.

This is preliminary information and CDC does not have firm evidence that infections have been caused by exposure to NECC products beyond the three previously listed lots of methylprednisolone acetate. Out of an abundance of caution, FDA has advised clinicians to follow up with patients to whom they have administered an injectable product, including an ophthalmic drug that is injectable or used in conjunction with eye surgery, and a cardioplegic solution purchased from or produced by NECC after May 21, 2012.

Clinicians should perform a thorough diagnostic evaluation to exclude infection in those patients who report signs and symptoms of infection following high-risk exposure to one of these NECC products (e.g., exposure of product to sterile body site). If the evaluation of these patients is suggestive of fungal infection, please consult existing CDC treatment guidance http://www.cdc.gov/hai/outbreaks/clinicians/index.html. Consultation with an infectious disease specialist is strongly encouraged to help make treatment decisions in these cases.

Products from NECC can be identified by markings that indicate New England Compounding Center by name or by its acronym (NECC), and/or the company logo that can be accessed here. Additional information about the MedWatch Safety Alert notice is available on the FDA website.

Recommendations for Clinicians

CDC and FDA have three recommendations for clinicians.

1. Clinicians should contact (by phone or in person) any patient who had an injection (e.g., spinal, joint) after May 21, 2012, using any of the following three recalled lots of preservative-free methylprednisolone acetate (80mg/ml) produced by NECC, to determine if they are having symptoms:
    - Methylprednisolone Acetate (PF) 80mg/ml Injection, Lot# 05212012@68, BUD 11/17/2012
    - Methylprednisolone Acetate (PF) 80mg/ml Injection, Lot#06292012@26, BUD 12/26/2012
    - Methylprednisolone Acetate (PF) 80mg/ml Injection, Lot# 08102012@51, BUD 2/6/2013

Symptoms that should prompt diagnostic evaluation include fever, new or worsening headache, neck stiffness, sensitivity to light, new weakness or numbness, increasing pain, redness or swelling at injection site. Some of the symptoms of patients who have ultimately been diagnosed with fungal meningitis have been mild and not classic for meningitis (e.g., new or worsening headache without fever or neck stiffness).

2. Healthcare professionals should cease use of **any** product produced by NECC, all of which have been recalled.

    - Through its investigation of the NECC facility, FDA cannot confirm the sterility of any of the NECC products. On October 15, FDA issued a MedWatch Safety Alert advising clinicians to follow-up with patients who received an injectable NECC product, including an ophthalmic drug that is injectable or used in conjunction with eye surgery, and a cardioplegic solution purchased from or produced by NECC after May 21, 2012. Clinicians are also requested to report any suspected adverse events following use of these products to FDA's MedWatch program at **1-800-332-1088** or www.fda.gov/medwatch

    As in the past, CDC continues to recommend that clinicians remain vigilant for any possible adverse events related to the use of any NECC product. Clinicians are encouraged to report such events to their state public health department.

3. CDC will continue to update clinical guidance as more information becomes available. As of October 16, CDC has updated clinician guidance addressing:

    - Interim Treatment Guidance for Central Nervous System (CNS) and/or Parameningeal Infections Associated with Injection of Potentially Contaminated Steroid Products
    - Interim Treatment Guidance for Septic Arthritis Associated with Injection of Potentially Contaminated Steroid Products
    - Interim Guidance for Management of Asymptomatic Persons Exposed to Potentially Contaminated Steroid Products
    - Diagnostic Testing for Septic Arthritis and Specimen Submission to CDC – Outbreak Associated with Injection of Potentially Contaminated Steroid Products
    - Instructions for Clinicians Regarding Diagnostic Testing and Specimen Shipping for Central Nervous System and/or Parameningeal Infections
    - Role of Antifungal Prophylaxis in Asymptomatic Patients

CDC Case Definitions

The current investigation is a rapidly evolving situation and information about cases continues to be updated. For the most recent information about case definitions, please see CDC's clinical guidance web page at http://www.cdc.gov/hai/outbreaks/clinicians/casedef_multistate_outbreak.html.

Additional Information

- Multistate Fungal Meningitis Outbreak Investigation
- MMWR Early Release: Multistate Outbreak of Fungal Infection Associated with Injection of Methylprednisolone Acetate Solution from a Single Compounding Pharmacy — United States, 2012.
- CDC HAN Advisory: Meningitis and Stroke Associated with Potentially Contaminated Product
- CDC HAN Advisory: Update: Multistate Outbreak of Meningitis and Stroke Associated with Potentially Contaminated Steroid Medication
- CDC Website on Fungal Diseases
- FDA Statement on Fungal Meningitis Outbreak

Facility Information

ALEGENT HEALTH BERGAN MERCY	7500 MERCY ROAD	OMAHA	NE
ALEGENT HEALTH PLASTIC	7710 MERCY ROAD SUITE 320	OMAHA	NE
ALEGENT WOMEN'S HEALTHCARE	11109 SOUTH 84TH STREET, SUITE 4800	PAPILLION	NE
COLUMBUS COMMUNITY HOSPITAL	4600 38TH STREET	COLUMBUS	NE
COLUMBUS SURGERY CENTER-	3772 43RD AVENUE SUITE B	COLUMBUS	NE
CREIGHTON MEDICAL CENTER	601 NORTH 30TH STREET	OMAHA	NE
EHRLING BERGQUIST HOSPITAL-	2501 CAPEHART ROAD	OFFUTT AFB	NE
FAITH REGIONAL HEALTH SERVICES	2700 W. NORFOLK AVE	NORFOLK	NE
FAITH REGIONAL HOSPITAL-CARDIO	2700 WEST NORFOLK AVENUE	NORFOLK	NE
FAITH REGIONAL SURGERY CENTER	301 NORTH 27TH STREET, SUITE 3	NORFOLK	NE
FAMILY PRACTICE OF GRAND ISLAND, P.C.	2116 W. FAIDLEY AVENUE, SUITE 400	GRAND ISLAND	NE
FREMONT AREA MEDICAL CENTER	450 EAST 23RD STREET	FREMONT	NE
GOOD SAMARITAN HOSPITAL.	10 E. 31ST STREET	KEARNEY	NE
HEARTLAND SURGERY CENTER	3515 30TH AVENUE	KEARNEY	NE
LAKESIDE HOSPITAL	16901 LAKESIDE HILLS COURT	OMAHA	NE
MEMORIAL COMMUNITY HEALTH, INC.	1423 7TH STREET	AURORA	NE
MEMORIAL HOSPITAL	1423 7th STREET	AURORA	NE
MIDWEST EYE SURGERY CENTER	4353 DODGE STREET	OMAHA	NE
NEBRASKA HEART HOSPITAL	7500 SOUTH 91ST STREET	LINCOLN	NE
NEBRASKA PAIN CONSULTANTS	6940 VAN DORN STREET	LINCOLN	NE
NEMAHA COUNTY HOSPITAL	2022 13TH STREET	AUBURN	NE
OGALLALA COMMUNITY HOSPITAL	2601 NORTH SPRUCE STREET	OGALLALA	NE
OMAHA AMB. SURGERY CENTER	825 N. 90TH STREET	OMAHA	NE
OUTPATIENT SURG SPECIALTIES CENTER LLC	11704 WEST CENTER ROAD, SUITE 110	OMAHA	NE
PHYSICIANS SURGICAL CENTER	1500 SOUTH 48TH STREET	LINCOLN	NE
PURE AESTHETIC MEDISPA	3610 RICHMOND CIRCLE	GRAND ISLAND	NE
SAINT ELIZABETH REGIONAL MED. CTR.	555 SOUTH 70TH STREET	LINCOLN	NE
SEWARD MEMORIAL HOSPITAL	300 NORTH COLUMBIA AVENUE	SEWARD	NE
SPINE & PAIN CENTER OF NEBRASKA, PC	9850 NICHOLAS STREET	OMAHA	NE
SURGERY CENTER OF FREMONT-	2727 NORTH CLARKSON STREET	FREMONT	NE
YORK GENERAL HOSPITAL	2222 NORTH LINCOLN AVENUE	YORK	NE